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LETTER

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AFIP signs collaborative agreements with Army, VA

Agreements pending with CDC, Ukraine

AFIP HAS ENTERED INTO FORMAL agreements with the U.S. Army Medical Research and Materiel Command (USAMRMC) and the Department of Veterans Affairs (VA) to provide mutually beneficial programs in consultation, education, and research, according to AFIP Director Michael J. Dickerson, Col, USAF, MC. "The Institute will now be working closely with USAMRMC in the area of infectious diseases, chemical or biological defense, and telemedicine," he says. "We're also pleased to formalize our relationship with the VA by serving as their special reference laboratory for pathology and providing services including consultation, cytopathology, specialized registries, and impartial peer review."

Florabel G. Mullick, MD, SES, AFIP Associate Director and Director, Center for Advanced Pathology, points out that the agreements couldn't come at a more appropriate time. "With increasing emphasis being placed on 'operations other than war' (OOTW), there's an increased likelihood of endemic infectious diseases becoming an even greater health problem for deployed U.S. Armed Forces," she notes. "We're also concerned about the possible use of chemical or biological agents."

Increased collaborations with USAMRMC and the VA help address these concerns, she points out. "We'll benefit from USAMRMC's strengths in biological, chemical, and infectious disease research, along with its expertise in telemedicine and other advanced technologies." The USAMRMC agreement emphasizes the effective use of resources, including scientific instrumentation, teaching programs, and transfer of technology developed at each organization. "Our primary goals will be to develop and evaluate telemedicine and telepathology in terms of cost, increased access to health care, and increased quality of care and to develop applications for the education of health care professionals using telemedicine technology. We'll be getting advice and support for our Telepathology Program from the Department of Defense (DoD)'s true pioneers," she notes.

The VA agreement enables AFIP to continue to provide consultation services on surgical cases under the Systematic External Review Surgical (SERS) Program, along with special reference services for VA pathologists. Included are AFIP's Prisoner of War and Persian Gulf War registries. The Institute will also provide cytopathology consultative services to VA pathologists, as requested, and establish a training program in cytopathology for VA pathologists and technicians.

The VA agreement, as coordinated and facilitated by Dr. Mullick and Theodore F. Beals, MD, National Director, Anatomic Pathology, Department of Veterans Affairs,

***Agreements**, continued on page 2*

Florabel G. Mullick, MD, SES, AFIP Associate Director and Director, Center for Advanced Pathology, observes as USAMRMC Commander Russ Zajtchuk, BG, MC, USA, signs the agreement.

DIRECTOR'S MESSAGE

Collaborating into the 21st Century

AFIP'S UNIQUE CIVILIAN AND MILITARY missions make us an ideal partner for new collaborative ventures, areas that we are exploring as the Institute looks towards the 21st century. Our cover story on recently-signed agreements with the U.S. Army Medical Research and Materiel Command (USAMRMC) and Department of Veterans Affairs (VA) highlights two of the many joint programs we have with other federal agencies.

Our strategic planning process, now in its final months, has identified a number of key issues that relate directly to our collaborative initiatives. Continued support for the Department of Defense (DoD) is being emphasized, particularly in the areas of readiness, provider education, and environmental pathology. We want to effectively utilize AFIP's expertise in pathology and the diagnosis of infectious diseases to support U.S. servicemembers stationed around the globe. Strengthening our ties to other DoD and federal agencies in the areas of medical intelligence, telemedicine, and preventive medicine is also essential.

AFIP's international reputation as a leader in diagnostic pathology, its scientific reference laboratories, the Office of the Armed Forces Medical Examiner (including the Armed Forces DNA Identification Laboratory) and its expertise in casualty identification, along with our National Tissue Repository and National Museum of Health and Medicine make the Institute a valuable resource for DoD, other federal agencies, and the civilian community. We look forward to establishing other collaborative agreements in the near future.

Have a happy holiday season and a rewarding 1997!

Michael J. Dickerson
Col, USAF, MC
The Director

***Agreements**, continued from page 1*

also includes support for the advancement of electronic applications for pathology and laboratory medicine and consultative services through the Institute's Telepathology Program. In exchange, the VA will provide AFIP with staff members to complete this vital mission.

Negotiations are also underway with the Centers for Disease Control and Prevention (CDC) for AFIP to provide expertise in the pathology and histologic diagnosis of infectious diseases and the identification of infectious agents to the CDC. The Institute, in return, will receive epidemiology and molecular diagnostic support from CDC. "We will benefit greatly from CDC's strength in epidemiology, and in turn AFIP will provide support in areas including tissue diagnosis, parasites, fungi, and other infectious diseases."

A fourth agreement, with the Ukraine, is expected to be formalized shortly. "This will allow AFIP and medical experts in the Ukraine to continue studies on the effects of the Chernobyl accident," Dr. Mullick notes.

AFIP laboratory receives CAP accreditation

The laboratory at the AFIP has been awarded a 2-year accreditation by the Commission on Laboratory Accreditation of the College of American Pathologists (CAP), based on the results of a recent on-site inspection.

AFIP Director Michael J. Dickerson, Col, USAF, MC, was advised of this national recognition and congratulated for the "excellence of the services being provided." AFIP's laboratory is one of the more than 4,600 CAP-accredited laboratories nationwide.

The CAP Laboratory Accreditation Program, begun in the early 1960's, is recognized by the federal government as being equal to, or more stringent than, the government's own inspection program.

Inspectors examine the records and quality control of the laboratory for the preceding 2 years, as well as the education and qualifications of the total staff, the adequacy of the facilities, the equipment, laboratory safety, and laboratory management to determine how well the laboratory is serving the patient.

The College of American Pathologists is a medical society serving more than 14,500 physician members and the laboratory community throughout the world. It is the world's largest association composed exclusively of pathologists and is widely considered the leader in laboratory quality assurance. The CAP is an advocate for high-quality and cost-effective medical care.

DoD DNA Registry division receives ISO 9001 Registration

Ted Anderson and Kim Smigielski preparing mock blood samples for proficiency test.

The Proficiency Test Operations Branch of the Department of Defense DNA Registry, a division of the Office of the Armed Forces Medical Examiner (OAFME), has been awarded ISO 9001 registration for its manufacture and design of proficiency test kits in both parentage and forensic testing.

"The ISO 9000 series is an international standard initiated in Europe to direct quality assurance needs, and we are honored to be a part of it," notes AFIP Director Michael J. Dickerson, Col, USAF, MC.

First envisioned by Victor W. Weedn, LTC, MC, USA, program manager, DoD DNA Registry, the proficiency testing program was developed in 1991 by Rhonda Roby, branch chief, Proficiency Test Operations Branch, for the forensic and parentage communities. The test is marketed by the College of American Pathologists. "AFIP's proficiency testing program allows laboratories that are involved in forensic and parentage testing to compare their test results," says Roby. "We manufacture a product that is distributed worldwide. Now, especially in Europe, ISO 9001 gives us this international recognition."

The DoD DNA Registry had to complete a series of standards and documentation in quality assurance in order to meet ISO 9001 standards. "Quality assurance really encompasses your whole operation," Roby points out, "including quality control, standard operating procedures, safety, and product maintenance. This was a tremendous team effort here at the laboratory."

Honored for their contributions in meeting ISO 9001 standards were: George C. Lin, former quality assurance officer; Theodore D. Anderson, chief quality assurance officer; Richard K. Lewis, quality assurance and safety coordinator; Marina Gregory, laboratory manager; Kimberly Smigielski, quality assurance officer; and program developer Roby.

Lymph Node Interpretation set for Saturday, April 26, 1997, at AFIP

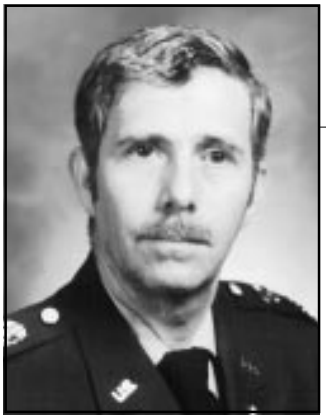
Lymph Node Interpretation, a one–day glass slide workshop for hematopathologists, general pathologists, pathology residents, and pathology fellows, will be held on Saturday, April 26, 1997, at AFIP. The workshop is designed to familiarize participants with important histologic and immunophenotypic findings in lymphoid lesions. "Participants will have the opportunity for hands–on study of predominantly lymph node and spleen lesions," notes course codirector Susan L. Abbondanzo, MD, chair, Department of Hematologic and Lymphatic Pathology. Approximately 150 cases will be available for review, and a microscope will be provided for each participant.

For each case, a clinical history, diagnosis, and description of salient morphologic and immunophenotypic features will be provided. The cases include a wide spectrum of reactive and neoplastic lesions. Short presentations will be given each hour to illustrate important diagnostic features.

The workshop will be held at AFIP's Radiologic Pathology Education Center, Bldg #53, on the grounds of Walter Reed Army Medical Center. For further information or to register, contact SrA Stephen Huntington at AFIP's Department of Education Services, (202) 782–5021.

PROFILES

Harvey P. Kessler, COL, DC, USA, Chair, Department of Oral and Maxillofacial Pathology



HARVEY P. KESSLER, COL, DC, USA, has been appointed chair, Department of Oral and Maxillofacial Pathology. The department serves as a consultation center for clinical, radiographic, and surgical pathology of the entire oral and maxillofacial apparatus, to include the hard tissues of the jaws, the oral and oropharyngeal mucosal soft tissues, the facial skin, and the skin and soft tissues of the neck. Specific areas of concentration and expertise include pathology of the major and minor salivary glands, the odontogenic apparatus, and benign fibro-osseous lesions of the bone. In addition, the department also provides forensic dentistry services and support for the Office of the Armed Forces Medical Examiner.

COL Kessler is a native of Baltimore, Md. He graduated from Case Western Reserve University in 1970, with a BA degree in chemistry. He received his DDS degree from the University of Maryland School of Dentistry in 1974. COL Kessler entered the U.S. Army immediately following dental school, completing a general practice residency at William Beaumont Army Medical Center in El Paso, Texas. Following a tour of duty at the United States Military Academy at West Point, he completed his training in oral and maxillofacial pathology at the U.S. Army Institute of Dental Research in Washington, DC, earning an MS degree in oral biology from George Washington University at the same time.

Following a fellowship in oral and maxillofacial pathology at AFIP, he served as chief, Oral Pathology and Oral Medicine at Fort Sill, Oklahoma; Ft. Knox, Kentucky; and Tripler Army Medical Center, Honolulu, Hawaii, and as a staff pathologist and chief, Forensic Dentistry, at AFIP. His most recent assignment was professor, Naval Dental School, National Naval Dental Center, Bethesda, Maryland. COL Kessler holds membership in the American Dental Association, the International College of Dentists, the American Academy of Oral and Maxillofacial Pathology, the American Academy of Forensic Sciences, and the American Academy of Oral Medicine.

COL Kessler is a diplomate of the American Board of Oral and Maxillofacial Pathology and the American Board of Oral Medicine. At present he is also the military consultant to the U.S. Army Surgeon General for oral and maxillofacial pathology, forensic dentistry, and HIV. He has authored or coauthored 13 scientific articles.

Markku Miettinen, MD, appointed Chair, Department of Soft Tissue Pathology

MARKKU MIETTINEN, MD, was recently appointed chair, Department of Soft Tissue Pathology. A native of Helsinki, Finland, Dr. Miettinen earned his MD degree at the University of Helsinki Medical School in 1977. Following his residency and board certification in anatomic pathology, Dr. Miettinen held the positions of attending pathologist and assistant professor of pathology in the Department of Pathology, University of Helsinki.

From 1984 to 1985, he served as a postdoctoral fellow and visiting scientist at Hahnemann University, Philadelphia, Pa.

Dr. Miettinen has held the positions of assistant professor, associate professor, and professor of pathology, anatomy and cell biology and of attending pathologist at the Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pa., since 1988.

He has authored or coauthored 135 original articles and 15 review articles on pathology, including a recent chapter on soft tissue tumors in *Anderson's Pathology*. His areas of special interest beyond soft tissue pathology include immunohistochemistry and molecular pathology\ and their application in tumor diagnosis and classification.

Dr. Miettinen is a member of several national and international societies, including the Arthur Purdy Stout Society for Surgical Pathologists, the International Academy of Pathology, and the College of American Pathologists.

He is an editorial board member on journals such as *Human Pathology, Virchows Archiv, Pathology Research and Practice, Applied Immunohistochemistry,* and *Journal of Urologic Pathology*.

PROFILES

Rosemary Kyte, LTC, MS, USA, appointed Director, Information Management

ROSEMARY KYTE, LTC, MS, USA, was recently appointed Director, Information Management at the AFIP. As such, she plans and directs Institute operations focused on "information as a resource": automation, telecommunications, visual information, and publications/records management. LTC Kyte comes to the AFIP from Fort Gordon, Georgia, where she served since 1994 as the chief information officer (CIO) to the Lead Agent, Department of Defense (DoD) Health Services Region 3, and as the CIO Southeast Regional Medical Command. While in these positions, she also served as chief, Information Management Division, Eisenhower Army Medical Center.

During her tour at Fort Gordon, LTC Kyte worked with telemedicine and multimedia technology, both of which have great potential for the AFIP. The medical center and the southeast region hosted the establishment of the Center for Total Access (CTA), which coordinates telemedicine efforts for the Army, working closely with DoD Health Affairs.

A native of Connecticut, LTC Kyte enlisted in the Army in 1975 as a research assistant at the US Army Research Institute of Environmental Medicine after graduating from the University of Connecticut with a BA degree in biology. She completed Officer Candidate School, the Airborne Course, and the AMEDD Officer's Basic Course in 1978, enroute to her first commissioned assignment in Korea as platoon leader, 2nd Medical Battalion, 2nd Infantry Division, Korea.

She spent the next 5 years in San Antonio, Texas, during which time she served as cadre at the Academy of Health Sciences and directed software projects. She then completed the AMEDD Officer Advanced Course and the Combined Arms Services Staff School, enroute to the 18th Medical Command (Korea), where she established their first Automation Management Office.

She is not entirely new to the area, having spent her next 4 years on the Walter Reed campus, 1986 to 1990, at the Army Office for Defense Medical Information Systems (DMIS). During this time she also completed an MS in computer science at Trinity University in San Antonio. In 1990, she returned to San Antonio as an instructor of information systems in the US Army-Baylor University Health Care Administration Program, and served there until her assignment to Fort Gordon in 1994.

Jerry D. Spencer, MD, JD, appointed as Armed Forces Medical Examiner

JERRY D. SPENCER, MD, JD, was recently appointed as the new Armed Forces Medical Examiner and Distinguished Scientist. Dr. Spencer replaces Dr. Charles Stahl, who retired on August 30, 1996.

Dr. Spencer has had two previous tours at the Armed Forces Institue of Pathology. While in the U.S. Navy, he did a residency in forensic pathology, and also served as a staff pathologist from 1979 to 1985. He was chief of the Division of Forensic Pathology and chairman of the Department of Forensic Sciences prior to his transfer to the U.S. Naval Hospital in Okinawa. After a 5-year tour in Okinawa, he was stationed at the U.S. Naval Hospital, Yokosuka, Japan, for 2 years before returning to the AFIP as Assistant Armed Forces Medical Examiner in the Office of the Armed Forces Medical Examiner. Dr. Spencer retired from the Navy as a Captain, Medical Corps, from the AFIP after 30 years service in 1993.

Dr. Spencer then went to Lubbock, Texas, where he organized a medical examiner's office for Lubbock County. He served as the Chief Medical Examiner for Lubbock County, and also was a clinical associate professor of pathology at the Texas Tech University School of Medicine for 3 years.

A native of Marysville, Kansas, Dr. Spencer graduated from Kansas State University and the University of Kansas Medical School. He also holds a law degree from the University of San Diego. He was a clinical intern, pathology resident, and staff pathologist at the U.S. Naval Hospital in San Diego before his first tour at the AFIP.

Dr. Spencer is a diplomate of the American Board of Pathology in anatomic, clinical, and forensic pathology. He has directed a residency program in forensic pathology during his assignments to the AFIP. He is a fellow of the American Academy of Forensic Sciences and the College of American Pathologists. He has also held faculty appointments at the Uniformed Services University of the Health Sciences and George Washington University.

Dr. Spencer and his wife, Nila, have four children. Their oldest daughter is an officer in the U.S. Navy, stationed aboard a destroyer. Two other daughters are in college, while their son is in high school.

MUSEUM

Stalking Ebola — artifacts in Museum trunk reveal strategies of the hunt

On May 6, 1995, the Centers for Disease Control and Prevention (CDC) were notified by Zairian public health authorities of a suspected outbreak of viral hemorrhagic fever in Kikwit, a city 240 miles east of Kinshasa, the capital of Zaire. Four days later, blood samples from 14 people were analyzed in Atlanta, confirming that the outbreak was caused by the Ebola virus.

The incubation period for Ebola is between 2 to 21 days. Early symptoms include fever, headaches, chills, myalgia, and malaise. The patient later gets severe abdominal pain with diarrhea and vomiting. In other reported outbreaks, between 50% and 90% of the cases have been fatal, the patient dying from severe internal bleeding. There is currently no treatment or vaccine for this virus.

Although the virus had been isolated in 1976, little was known about the mode of transmission. The Government of Zaire invited the CDC to send a team of three epidemiologists to help contain the virus, collect specimens, study the clinical course of the disease, and try to identify the source of the infection. In June 1996, the National Museum of Health & Medicine received one of the original trunks used to send supplies with the CDC team to Kikwit, Zaire. The artifacts inside that Rubbermaid™ trunk tell the story of how epidemiologists studied the Ebola virus.

Ebola can be spread through contact with infected blood and other body fluids. Outer garments worn by team members were standard operating room attire, such as waterproof surgical gowns with face shields. Since laboratory work with this virus requires a biosafety level four containment, special equipment was required for work in the field. Members of the team wore Racal Air-Mate Hepa 12 air-purifying personal respirators. A respirator headpiece and air hose was donated to the Museum collection. The headpiece covered the face and had an attachment for a hose that ran to a belt-mounted air filter unit, which inflated the headpiece to ensure the wearer did not inhale air containing the virus. A wash bottle filled with 70% ethyl-alcohol was used to disinfect blood and body fluid spills.

Skin biopsy kit.

The first phase of the CDC operation was active surveillance of the local population within a 150-mile radius of Kikwit. The trunk's contents included an example of a straw hat worn by Zairian, American, or World Health Organization health care workers who went into the communities to identify possible patients infected with Ebola. There is an example of a blood drawing kit, which contained vacutainers, tourniquets, latex gloves, and a small sharps container, and was used to collect blood samples that were diagnosed using an ELISA test for Ebola developed by CDC.

The trunk also contains a sample skin biopsy kit, something the CDC developed to collect specimens after the virus was found in the skin. These kits contained latex gloves and masks for the doctor, along with powdered bleach disinfectant. The specimen - collected using a disposable biopsy punch then fixed in a vial containing formalin - would be sent to the CDC in an enclosed mailing tube through the regular U.S. mail. The kit included instructions for getting specimens to the U.S. Embassy. The skin biopsy technique was safer and easier than drawing blood, since it eliminated the risk of accidental needle sticks.

The other mission assigned to the CDC team was to identify the Ebola virus vector and reservoir. Although primates were involved in the three previous outbreaks, it was not clear if they were the source of the virus or if the virus had been transmitted to them from another vector. Traps were set to catch animals in the area surrounding Kikwit. A fine black nylon net was used to catch small birds. Small metal traps were used to catch rodents and other tiny animals. CDC scientists examined the animals caught, took basic measurements, and recorded information about trap location as well as a description of the habitat.

Examples of traps and the animal sampling kits developed by CDC to collect tissue specimens from the captured animal are among trunk contents. The kit—a plastic bag—contains an anesthetic, supplies and equipment for blood sampling, and vials for storing the samples. Once caught, the animal was placed in the plastic bag and anesthetized. A blood sample was obtained from a rear corner of the eye with the enclosed capillary tube that ran into a cryovial. Lung tissue samples were placed in another cryovial, and all were routed to the CDC in Atlanta for analysis.

Once the outbreak had been contained, the CDC team returned to Atlanta to

***Ebola**, continued on page 7*

AFIP seeks collaborators for aerospace and/or hyperbaric environmental research

The Armed Forces Institute of Pathology (AFIP) is seeking collaborators in research related to the aerospace environment and/or the hyperbaric environment (either diving or clinically related). Research questions related to readiness and casualty evacuation are preferred.

AFIP's Division of Altitude & Hyperbaric Physiology, Department of Scientific Laboratories, is dedicated to enhancing the scientific understanding of the effects of oxygen on biological systems at high and low atmospheric pressures.

The Division of Altitude and Hyperbaric Physiology is staffed by three experienced PhD officers and five aerospace physiology technicians. The division has four laboratories: a hyperbaric (dive) chamber laboratory, a hypobaric (altitude) chamber laboratory, a molecular biology laboratory, and a tissue culture laboratory. Completed research includes the following:

1. In the study "Visual Performance with Aviator Night Vision Imaging System (ANVIS) at High Altitude (4300 meters)," test subjects demonstrated no impairment in visual acuity or contrast sensitivity when using night vision goggles in two different simulated night sky conditions. There was a significant difference in the pO2 levels of males vs females.

2. "Combined Effects of Hyperbaric Oxygen and Antimicrobials in a Mouse Model of Gas Gangrene" demonstrated that either clindamycin or metronidazole significantly prolonged survival of *Clostridium*-infected mice more than penicillin, imipenem, or sham treatment. The addition of hyperbaric oxygen treatments did not significantly affect survival.

3. Hyperbaric oxygenation was found to potentiate the in vitro killing effects of amphotericin B against *Leishmania* promastigotes in the study entitled "Augmented Oxygen-Dependent Killing of Leishmania."

One current protocol involves examining the effects of space flight on muscle cell growth in vitro. Changes in cellular morphology were observed after cells were flown aboard the space shuttle. In addition, these cells failed to fuse to form myofibers. In another current protocol, a new model for soft tissue radionecrosis is being developed. This model will be used to evaluate the efficacy of hyperbaric oxygen therapy in treatment.

Those interested in collaborative research efforts related to the aerospace or hyperbaric environments should contact Captain David Kulesh, PhD, USAF, (202) 782-2652, DSN 662-2652, or Internet: <kulesh@email.afip02.osd.mil> .

***Ebola**, continued from page 6*

evaluate the mountain of data accumulated during the expedition. While much of the epidemiology of Ebola remains a mystery, the recent outbreak had given scientists an unprecedented opportunity to study this rare and deadly disease.

Donation of these materials to Museum collections not only provides the means for us to document the methods of epidemiological research conducted by the CDC in Zaire, but it affords the National Museum of Health & Medicine a unique opportunity to preserve history in the making. The NMHM acknowledges the assistance of John Parascandola, PhD, Office of the Public Health Historian, USPHS, and Bertha Farrar, Special Pathogens Branch, CDC.

Use of trade names is for identification only and does not imply endorsement of the Public Health Service or HHS.

HISTOTECHNOLOGY NOTES

HELPFUL HINT: Eliminating Bubbles from Aqueous Coverslipping

When coverslipping slides with water-soluble mounting medium, heat aqueous medium while slightly warming slides on a moderate temperature slide warmer, then place a drop of heated medium on a slide and coverslip. This will prevent bubbles.

HELPFUL HINT: A Rapid Method for Removing Coverslips

A rapid method for removing coverslips in slides that have been covered for years is to lay slides on crushed dry ice in a small ice chest for 1 to 2 minutes. Pop off coverslip quickly and easily with no loss of tissue.

Placing slides in acetone for several minutes before clearing in xylene makes removal of residual mounting media faster and keeps xylene clean for a longer time period.

This article appeared in *Navy Medicine*, Vol 87, No 3, May-June 1996.

Errors in Pap Smear Interpretation: What Every Provider Should Know

by LCDR C. W. Ollayos, MC, USN
Armed Forces Institute of Pathology

Introduction. The Papanicolaou ("pap") smear is one of the greatest weapons in the war against cancer. This well-known medical test has helped save thousands of lives since Dr. George Papanicolaou (1883-1962) introduced it in 1943 (1). However, failures in pap smear testing do occur.

The Pap Smear Test. The pap smear is a test performed on part of the female genital tract called the uterine cervix. The pap smear can detect several types of infectious agents, including bacteria, viruses, and parasites. The pap smear will also occasionally detect several types of cancer from the vagina, endometrium, ovary, and fallopian tube. Most importantly, however, the pap smear is used to screen for cancerous and precancerous lesions of the cervix itself.

Cervical Cancer. As recently as the 1940s, cervical cancer was the leading cause of cancer deaths in women in the United States. However, annual deaths from cervical cancer have been dropping, mostly due to the widespread use of screening pap smears. Still, it is estimated that there will have been about 16,000 new cases and 5,000 deaths from cervical cancer in 1995 (2).

Several types of cancer can occur at the cervix. Numerically, however, one type is by far the most significant. This is squamous cell carcinoma. Fortunately, the pap smear is most able to detect this type of cancer.

HPV Infection and Squamous Cell Carcinoma of the Cervix. In at least 90% of cases, squamous cell carcinoma of the cervix appears to be caused by an infection with human papillomavirus (HPV) (3). HPV has many strains, only a few of which have been closely linked to subsequent development of cervical carcinoma. HPV infection can cause a variety of squamous cell changes that can be detected on pap smear.

Classification of HPV-Related Changes. The "Bethesda System," developed in 1988 (4) and modified in 1991 (5), is now the most widely used classification system. This system groups the precursor lesions of squamous cell carcinoma into two groups. The first tier is called low-grade squamous intraepithelial lesion (LSIL). This category includes the previously used terms of koilocytosis, koilocytic atypia, HPV effect, cervical intraepithelial neoplasia (CIN) 1, and mild dysplasia. The second, more severe tier, is called high-grade squamous intraepithelial neoplasia (HSIL). This category includes the previously used terms of CIN 2, CIN 3, moderate dysplasia, severe dysplasia, and carcinoma in situ.

Errors and the Pap Smear. The strength of the pap smear is simply that it works most of the time. Unfortunately, in a small percentage of patients the pap smear interpretation will not reflect what is actually happening in the patient.

Two types of errors occur in pap smear interpretation. The first is called a false-positive error. This means the pap smear is interpreted as abnormal, but the patient is healthy. The second type of error is called a false-negative error. This means the pap smear is interpreted as normal (or perhaps as having benign reactive changes), but the patient really has a significant lesion.

One large study found the major discrepancy rate in pap smear interpretation to be 5% (6). The results were broken out further to reveal a false-positive rate of 5.1% and a false-negative rate of 4.2%. However, these figures probably represent the best case scenario because the participants were aware they were being tested and may have exercised extraordinary care when reviewing the smears. In other studies, the false-negative rate has been repor
ted to be in the range of 5% to 67% (7).

There are several reasons why any single pap smear might fail to identify a disease process (8). These are:

1. No diagnostic cells are on the slide because the lesion might not be shedding cells.
2. No diagnostic cells are on the slide because they lie in a hard-to-reach location.
3. The lesional cells might be overlooked or misinterpreted by the laboratory staff.
4. The lesional cells might be obscured by poor fixation, blood, or inflammation.

Reasons # 1 and 2 above are generally grouped and referred to as "sampling error." Reason # 3 above is generally referred to as "screening error" or "interpretation error." The literature generally supports the notion that most "misses" are due to sampling error (9).

The Bottom Line. Errors occur in pap smear screening, even among the best clinicians and the best cytology laboratories. The innate qualities of the test make perfection impossible. Despite its limitations, the cervical pap smear remains the best tool available for the detection of squamous cell carcinoma of the cervix and its precursors. The way to make the pap smear a better test is to do more of them. If a patient has three normal pap smears over a 3-year period, the false-negative rate drops to a very respectable 2% (8).

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REPOSITORY AND RESEARCH SERVICES

AFIP's National Tissue Repository – a significant public health resource

Sending cases from overseas? Please follow these guidelines

The AFIP often receives calls from various airports on the east and west coasts concerning packages sent from overseas. Occasionally, we are not able to provide enough information based on the package label to United States customs agents to allow the package to be forwarded to the Institute. The package is then returned to the contributor. In order for a package from overseas to pass through U.S. Customs, the following information should be provided on the package label: a detailed description of the contents; a statement that the material is noninfectious and noncontagious; whether the material is derived from humans or animals; and from what part of the body the tissue is derived. Questions concerning cases being forwarded from overseas can be addressed to the administrator, Repository and Research Services, at (202) 782-2500.

For our military and federal contributors, the AFIP receives a large number of slide containers on a daily basis, much more than we can use ourselves. If your facility regularly submits cases to the Institute and would like some of these holders to be returned, please call the administrator, Repository and Research Services at the above number and specify the type and number of slide holders you need. We will do our best to accommodate your request.

Construction on the Repository addition will be completed by June 1997.

Groundbreaking recently took place for a new 16,000 square foot addition to the AFIP National Tissue Repository. The repository consists of over 2.5 million cases accessioned to the Institute since 1917. These cases consist of a variety of materials that can include written reports, clinical histories, x-rays, photographs, photomicrographs, 35-mm slides, microscopic glass slides, paraffin blocks, formalin-fixed tissue, and follow-up information. Our current facility for housing this material is almost filled to capacity.

Between 50,000 to 60,000 new cases are accessioned each year from all over the world, representing both sexes, all races/ethnicities, and all ages. Approximately 20% of newly accessioned cases are cancer. The rest of the cases represent the entire spectrum of human and animal diseases.

The new repository addition will be used to accommodate the current and future growth of our repository as well as serve as the main storage area for pathologic material received from closed military medical facilities. The Institute receives a number of retrieval requests each month for material we are holding from these facilities. This material is being temporarily stored at two separate warehouse facilities, one in Gaithersburg and one in Silver Spring, Maryland. We currently are storing material from 14 closed facilities.

Given this volume, the AFIP repository represents a significant public health resource. Repository specimens can be used to identify cases for nested case-control studies or cohorts of cases for prospective studies of unusual tumors or conditions. Cases collected at the AFIP can be used to serve as a barometer of disease as part of a public health surveillance system. The AFIP repository is also an appropriate location for the storage of pathologic material obtained from multicenter medical and epidemiologic studies. The Institute is currently exploring ways to make best use of this valuable resource to include participation in collaborative efforts requiring the unique resources of the National Tissue Repository. Consideration is being given to the development of a frozen tissue repository.

The AFIP has a public trust to both preserve and use these specimens for the improvement of our nation's health. As such, we are looking forward to the completion of our repository addition by the end of June 1997. Questions concerning the use of repository materials in approved studies should be directed to Dr. Michael R. Peterson, chair, Department of Repository and Research Services, at (202) 782-2647 or e-mail to peterson@email.afip.osd.mil.

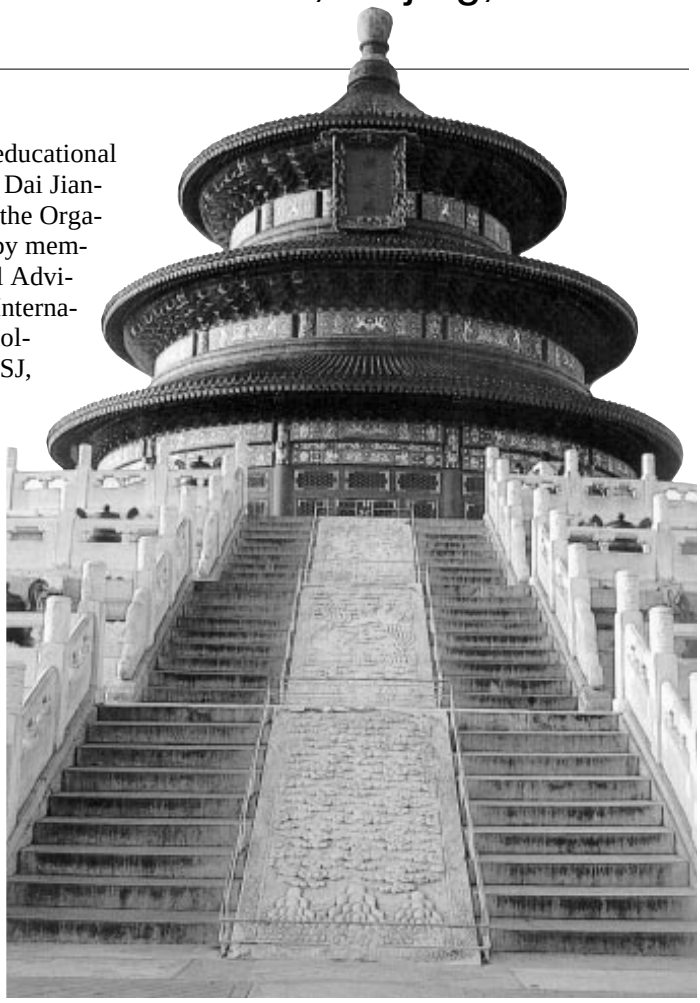
Department of Radiologic Pathology staff represent AFIP at 19TH INTERNATIONAL CONGRESS OF RADIOLOGY, Beijing, China

Members of the Department of Radiologic Pathology had the privilege of representing the Armed Forces Institute of Pathology at the 19th International Congress of Radiology that took place in Beijing, The People's Republic of China, from 9 to 13, June 1996. Anne G. Osborn, MD, Nycomed professor of diagnostic imaging at the AFIP and former Distinguished Scientist organized a comprehensive course in Radiologic-Pathologic Correlation, which was presented to over 4,000 radiologists from the People's Republic of China and 42 other countries. The following members of the Department of Radiologic Pathology participated as course faculty: Geoffrey A. Agrons, MD, chief, Pediatric Radiology; James L. Buck, MD, former chair and registrar; Mark D. Murphey, MD, chief, Musculoskeletal Radiology; Melissa L. Rosado de Christenson, Lt Col, USAF, MC, chair and registrar and chief, Pulmonary and Mediastinal Radiology; James G. Smirniotopoulos, MD, chief, Neuroradiology; and Brent J. Wagner, MD, chief, Genitourinary Radiology. Additional faculty included Pablo R. Ros, MD, Leonard M. Glassman, MD, Diane C. Strollo, MD, and Donald Resnick, MD.

The above radiologists participate extensively in the educational programs of the Department of Radiologic Pathology. The course curriculum consisted of 69 hours of didactic instruction in diagnostic imaging with an emphasis on radiologic-pathologic correlation. These lectures were especially well received by the predominantly Chinese audience, as autopsies are not performed in their country. Thus, Chinese radiologists, for the first time, were presented with material dedicated to understanding how the gross morphology of disease results in specific radiologic abnormalities using the vast spectrum of diagnostic imaging modalities.

The quality of the educational program was lauded by Dai Jianping, MD, chairman of the Organizing Committee and by members of the International Advisory Committee to the International Congress of Radiology. Otha W. Linton MSJ, executive director of the International Society of Radiology, expressed his deep appreciation of the department's contribution to the Congress in a letter to Colonel Michael J. Dickerson, The Director, AFIP.

The Department of Radiologic Pathology is committed to excellence in radiologic education. Currently, 307 diagnostic radiology residency programs send their residents to our 6-week-long Radiologic Pathology Courses. In addition, six short courses are offered annually throughout the United States, designed for radiologists who have completed their residency and other practicing physicians. International courses are held each year in Mexico, Austria, Portugal, and Spain. The Mexico course is held in collaboration with the Mexican Army Medical Corps in the Central Military Hospital of Mexico City. As the department continues to expand the scope of its educational mission, new annual courses will be held in France in 1996 and in Germany, Canada, and Brazil in 1997. These programs will disseminate the concepts of radiologic-pathologic correlation studied at the AFIP to an ever-increasing number of radiologists and physicians throughout the world.



The Temple of Heaven, Beijing. *Photo by Magnus Barttlett, from Passport Books, a division of NTC Publishing Group.*

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Uropathology	27–31 January 97	DoubleTree Hotel, Rockville, MD
Thoracic Radiologic Pathologic Review	3–7 February 97	AFIP, Washington, DC
Neuroradiology Review	22–23 February 97	Hyatt Regency, Bethesda, MD
35th Annual Neuropathology Review	24–28 February 97	Hyatt Regency, Bethesda, MD
33rd Annual Forensic Dentistry	3–8 March 97	Hyatt Regency, Bethesda, MD
34th Annual Basic Science Course in Otolaryngology/ Head & Neck Surgery	3–28 March 97	USUHS, Bethesda, MD
43rd Annual Course in Oral Pathology	1–4 April 97	Hyatt Regency, Bethesda, MD
Women's Imaging	5–6 April 97	**Menger Hotel, San Antonio, TX**
Abdominal & Pelvic Imaging Review	12–13 April 97	Washington Marriott, Washington, DC
Interdisciplinary Course on Breast Disease	25–26 April 97	TBA, Georgetown University, Washington, DC
Lymph Node Interpretation: A Glass Slide Workshop	26 April 97	AFIP, Washington, DC
7th Anatomic Pathology Update & Review	11–17 May 97	TBA, Georgetown University, Washington, DC
Musculoskeletal Imaging Weekend	17–18 May 97	**Loew's Hotel, Annapolis, MD**
Descriptive Veterinary Pathology	TBA 97	Natcher Ctr., NIH, Bethesda, MD
10th Annual Forensic Anthropology	9–13 June 97	USUHS, Bethesda, MD
Genitourinary Radiology	14–18 July 97	AFIP, Washington, DC
Congenital DNA Repair Deficiency in Humans	20–21 July 97	**TBA, Poughkeepsie, NY**
Musculoskeletal Radiology	21–25 July 97	AFIP, Washington, DC
Neuroradiology	4–8 August 97	AFIP, Washington, DC
44th Annual Pathology of Laboratory Animals	11–14 August 97	Natcher Ctr., NIH, Bethesda, MD
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Radiologic Pathologic Correlation	5–9 October 97	**George Washington Inn & Conference Ctr., Williamsburg, VA**
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Abstracts of Recent Publications by AFIP Staff

Replication of HIV-1 in dendritic cell-derived syncytia at the mucosal surface of the adenoid

Sarah S. Frankel, Bruce M. Wenig, Allen P. Burke, Poonam Mannan, Lester D. R. Thompson, Susan L. Abbondanzo, Ann M. Nelson, Melissa Pope, Ralph M. Steinman

Human immunodeficiency virus-type 1 (HIV-1) replicates actively in infected individuals, yet cells with intracellular depots of viral protein are observed only infrequently. Many cells expressing the HIV-1 Gag protein were detected at the surface of the nasopharyngeal tonsil or adenoid. This infected mucosal surface contained T cells and dendritic cells, two cell types that together support HIV-1 replication in culture. The infected cells were multinucleated syncytia and expressed the S100 and p55 dendritic cell markers. Eleven of the 13 specimens analyzed were from donors who did not have symptoms of acquired immunodeficiency syndrome (AIDS). The interaction of dendritic cells and T cells in mucosa may support HIV-1 replication, even in subclinical stages of infection.

Science. 1996;272:115-117.

Atypical features in salivary gland mixed tumors: their relationship to malignant transformation

Paul L. Auclair, DMD, MS, and Gary L. Ellis, DDS

Although criteria for distinction between the benign and malignant elements in carcinoma *ex* mixed tumor have been adequately described, there have not been any attempts to identify clinical or histologic features in benign mixed tumors that indicate increased risk of malignant change. For this reason, 65 mixed tumors of the major and minor salivary glands that exhibited atypical histologic features were examined in an attempt to analyze which, if any, of these features might indicate a greater likelihood of malignant transformation. The atypical features evaluated were hypercellularity, capsule violation, hyalinization, necrosis, and cellular anaplasia. The mitotic rate was also analyzed. The age of the patient, and the site, size, and prediagnostic duration of the tumor were recorded and, together with the histologic findings, were correlated with follow-up information. Nine (13.8%) of the 65 tumors underwent malignant transformation. Five of these patients died of the tumor, two others had distant metastases and were alive with the disease, and two were free of disease. Benign mixed tumors that showed prominent zones of hyalinization or at least moderate mitotic activity were more likely to develop carcinoma than those that did not. $_X^2$ analysis indicated that only hyalinization was significant ($P < 0.05$), but, with Fisher's exact test (two-tailed), this and all of the other features evaluated revealed a P value greater than 0.05. The other atypical features failed to correlate with malignant change. Clinical findings at the initial diagnosis that indicated a greater likelihood of malignant transformation were occurrence in the submandibular gland, older patient age, and large tumor size.

Mod Pathol. 1996;9(6):652-657.

Olfactory neuroblastoma and other round cell lesions of the sinonasal region

Kenneth Devaney, MD, Bruce M. Wenig, MD, Susan L. Abbondanzo, MD

Sixty-nine round cell lesions of the sinonasal region (22 olfactory neuroblastomas [ONBs], 17 malignant lymphomas, nine Ewing's sarcomas [ES], nine rhabdomyosarcomas, three sinonasal undifferentiated carcinomas, five malignant melanomas, and four pituitary adenomas) were studied in an attempt to define the differential diagnostic capabilities of antibody to MIC2 and bcl-2 in paraffin-embedded tissue in the distinction of these lesions. In addition, antibody to p53 was applied in each case to define the incidence of p53 positivity among these various tumor types. Each of the ES cases was MIC2 positive; each of the other cases was MIC2 negative. Positivity for bcl-2 was confined to two cases, one of them a malignant lymphoma (85% of cells positive) and one an ONB (5% of cells positive). Small numbers of scattered p53-positive cells appeared in the majority of cases studied, without regard for the specific tumor type; only a single case, a malignant lymphoma, showed a majority (approximately 90%) of p53-positive cells. These results indicate that the MIC2 antibody is a useful method by which to distinguish ES from a variety of other round cell lesions that may be encountered in the sinonasal region. The practical applications of antibody to bc1-2 and p53 seem to be much more limited; by contrast, neither bcl-2 positive cells nor abundant p53 cells identified by immunohistochemical analysis seemed to be frequent findings in any of the tumor types studied. Although ONBs have been included with the peripheral primitive neuroectodermal tumors for classification purposes, these tumors diverge from the ES/primitive neuroectodermal tumor family in that they do not seem to share either the MIC2 positivity or the t(11;22) chromosomal translocation that typify the ES/primitive neuroectodermal tumor family of lesions. Although bcl-2 positivity has been associated with a light snicro-scopic finding of an unfavorable histologic pattern in retroperitoneal neuroblastomas, it does not seem that bc1-2 positivity in ONB will select for a clinically distinctive subset of patients. carcinoma

Mod Pathol.1996;9(6):658-663.

Calcium oxalate crystals in human pathology: molecular analysis with the laser Raman microprobe

Joseph P. Pestaner, MD; Florabel G. Mullick, MD; Frank B. Johnson, MD; Jose A. Centeno, PhD

Objective.—Calcium oxalate crystals in pathologic specimens were examined by the laser Raman microprobe, a nondestructive spectroscopic technique. Although research focused on the identification of calcium oxalate deposits in tissue sections, kidney stones were also studied to determine the in situ structural specificity of the technique.

Design.—Paraffin-embedded tissue specimens were cut into sections of 2 to 6 µm. The unstained sections were placed on metal (aluminum)-plated slides and excited with the 514.5-nm line of an argon-ion laser, which was focused to a 1-µm spot size using a high-resolution optical microscope.

Main Outcome Measure.—The laser Raman microprobe technique generates spectra that differentiate the monohydrate (CaC_20_4-H_2O, whewellite) and the dihydrate (CaC_20_4-$2H_2O$, weddellite) forms of calcium oxalate inclusions in tissue sections.

Results.—Characteristic spectra were generated and provided unequivocal evidence for the identification of the dihydrate oxalate form of calcium oxalate crystals in cases of oxalosis of the myocardium and for the monohydrate oxalate structure in a case of oxalosis of the pituitary. Finally, the combined occurrence of both oxalate structures was confirmed in kidney stone specimens.

Conclusion.—The results obtained in this investigation demonstrate the efficacy of the laser Raman microprobe as a useful adjunct in diagnostic pathology.

Arch Pathol Lab Med. 1996;120:537-540.

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1. Auclair PL, Ellis GL. Atypical features in salivary gland mixed tumors: their relationship to malignant transformation. *Mod Pathol*. 1996;9:652-657.
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